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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/673,426	09/30/2003	Jen-Wei Chiao	15741.003	2704

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EXAMINER	
CARTER, KENDRA D	
ART UNIT	PAPER NUMBER
1617	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/673,426	CHIAO ET AL.	
	Examiner	Art Unit	
	Kendra D. Carter	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25 and 27-28* is/are rejected.

7)☒ Claim(s) *26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/30/03; 12/10/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claim 26 is objected to because it is dependent on the rejected claims 16 and 22 by Moore et al. (US 2002/0164694 A1).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(1) Claims 1, 3, 4, 6, 8, 13, 14, 16, 19, 20, and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Sherr et al. (US 6,407,062 B1).

Sherr et al. teaches a method of treating a mammal that has a tumor and/or cancer by administering a composition comprising a pharmaceutically acceptable carrier and ARF-p19 fragment or a related compound that can act as a tumor suppressor in the cell (see column 8, lines 59-65; address applicant's claim 1 in part). In such embodiment the INK4a exon 1α and the tandemly linked INK4b locus remain intact, so that the cell does not express endogenous exon 1β, but can express p16INK4a (see

column 9, lines 60-63; address applicant's claims 21, 23 and 24). INK4A gene encodes a specific inhibitor (INK4a-p16) of the cyclin D-dependent kinases CDK4 and CDK6. INK4a-p16 can block these kinase from phosphorylating the retinoblastoma protein (pRb), preventing exit from the G1 phase of the cell cycle (see abstract, lines 1-5; address applicant's claim 25 and claim 28 in part The composition can be administered orally or intravenously (see column 36, lines 11-12, 16, and 18; address applicant's claim 14). The conjugated targeting molecules to the ARF-p19 fragment is administered *in vivo* and can be a peptide, protein or antibody (see column 36, lines 30-36; address applicant's claims 1 in part and claim 28). The antibodies are specific cell surface antigen, for example the tumor cell (see column 36, lines 45-48; address applicant's claim 8 in part and claims 13 and 19). The antibody compositions are labeled with isothiocyanate (see column 34, lines 12-13 and 16-17; address applicant's claim 1 in part). The antibody is a protein molecule synthesized by a B-cell upon exposure to antigen capable of combining specifically with that antigen (see column 22, lines 15-17; address applicant's claims 3, 8 and 16 in part). The antigen is a molecule or composition of matter which (1) induces an immune response in an animal, and (2) interacts specifically with antigen-recognized components of an immune animal's immune system (see column 22, lines 27-30; address applicant's claim 1 and 16 in part). The antigenic portion of the molecule can be that portion that is immunodominant for antibody or T cell receptor recognition, or it can be a portion used to generate an antibody to the molecule by conjugating the antigenic portion to a carrier molecule for immunization (see column 22, lines 36-39; address applicant's claim 4). The diseases

treated are those that include any abnormal condition or an organism or par especially as a consequence of infection, including cancers and tumors (see column 22, lines 59-64; address applicant's claim 6).

(2) Claims 1, 6-8, 10-14, 16, 19, and 21-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Moore et al. (US 2002/0164694 A1).

Moore et al. teaches antibodies or fragments thereof conjugated to a diagnostic or therapeutic agent (see page 42, paragraph 254, lines 1-3) such as isothiocyanate (see page 42, paragraph 254, column 2, lines 9-10; address applicant's claim 1 in part). The invention stimulates lymphocyte B cell proliferation, differentiation and/or activation (see page 63, paragraph 454, lines 2-3; address applicant's claims 1, 8 and 16 in part), which is transformed from human peripheral blood (see page 36, paragraph 217, lines 6-7; address applicant's claim 1 and 8 in part). Selection procedures can be performed to enrich the sample for B cells that are antigen-reactive (see page 36, paragraph 217, lines 11-13; address applicant's claim 21). The polyclonal antibodies to an antigen-of interest can be produced by various procedures well known in the art (see page 36, paragraph 213, lines 2-4; address applicant's claims 8, 13, 16 and 19 in part). The compounds are useful for the treatment of various immune system-related disorders, including cancers (see page 48, paragraph 307, line 3; address applicant's claim 6 and claims 8 and 19 in part) and AIDS (i.e. insufficient T-cell function; see page 32, paragraph 175, line16 and page 50, paragraph 331, line 4; address applicant's claim 7

and claim 12 in part) as well as infectious diseases (see page 32, paragraph 175, line 8; address applicant's claim 6 and 13 in part) in mammals, preferably humans (see page 48, paragraph 311, lines 1-3; address applicant's claims 1 in part). The treatment increase the immune response, particularly increasing the proliferation and differentiation of B cells. The immune response may be increased by either enhancing an existing immune response or by initiating a new immune response (see page 51, paragraph 336 lines 4-8; address applicant's claim 1 in part). The composition may be administered alone or in combination with other therapeutic agents such as chemotherapeutic agents and conventional immunotherapeutic agents (see page 55, paragraph 383, lines 1-6; address applicant's claims 10 and 20). The composition may be administered with a vaccine (see page 55, column 2, lines 1-2; address applicant's claim 11 and 22). The composition can be administered orally, topically, or intravenously (see page 53, paragraph 354, lines 5-6 and paragraph 361, lines 1-4; address applicant's claim 14).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

(1) Claims 2, 15, 17, and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062 B1) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above and in view of Ghai et al. (US 5,955,269).

Sherr et al. teaches are as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above.

Sherr et al. does not teach a method wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or phenethyl isothiocyanate (PEITC) disclosed in applicant's claims 2, 17, 27, and 28, or wherein the ITC-based agent is administered systemically in a dietary composition or supplement as disclosed in applicant's claim 15.

Ghai et al. teaches a method for identifying nutraceuticals that can be used with any food of food substance to be incorporated in to composition which may be administered to a subject to treat or prevent a disease or undesirable condition (see abstract in its entirety; address applicant's claim 15 in part) by up-regulating the expression of one or ore genes that contribute to maintaining or improving the health of the subject, such as by preventing the disease (see column 3, lines 54-55 and 59-61). The nutraceutical phenethyl isothiocyanate is isolated from watercress (see column 24, table I, line 6; address applicant's claims 2, 17, 27 and 28 in part). The composition can be formulated to a food supplements (see column 25, lines 21-22; address applicant's claim 15) or processed food (see column 26, lines 43-44).

To one skilled in the art at the time of the invention would have found it obvious to combine the method of Sherr et al. and wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or phenethyl isothiocyanate (PEITC) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement because Ghai et al. teaches a method of treating diseases by administering phenethyl isothiocyanate in a dietary composition or supplement (see abstract in its entirety; column 24, table I, line 6; column 25, lines 21-22; and column 26, lines 43-44).

The motivation to combine the method of Sherr et al. and wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or

phenethyl isothiocyanate (PEITC) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement is because Ghai et al. teaches that PEITC treats diseases by activating the immune system (see column 3, lines 54-55 and 59-61). Additionally, Ghai et al. teaches that PEITC is isolated from a food substance and can be administered in processed foods or supplements.

(2) Claim 2, 15, 17, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. (US 2002/0164694 A1) as applied to claims 1, 6-8, 10-14, 16, 19, and 21-22 above and in view of Ghai et al. (US 5,955,269).

Moore et al. (US 2002/0164694 A1) teachings are as applied to claims 1, 6-8, 10-14, 16, 19, and 21-22 above.

Moore et al. does not teach a method wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or phenethyl isothiocyanate (PEITC) disclosed in applicant's claims 2, 17, and 20 or wherein the ITC-based agent is administered systemically in a dietary composition or supplement as disclosed in applicant's claim 15.

Ghai et al. teaches a method for identifying nutraceuticals that can be used with any food of food substance to be incorporated in to composition which may be administered to a subject to treat or prevent a disease or undesirable condition (see

abstract in its entirety; address applicant's claim 15 in part) by up-regulating the expression of one or ore genes that contribute to maintaining or improving the health of the subject, such as by preventing the disease (see column 3, lines 54-55 and 59-61). The nutraceutical phenethyl isothiocyanate is isolated from watercress (see column 24, table I, line 6; address applicant's claims 2, 17, and 20 in part). The composition can be formulated to a food supplements (see column 25, lines 21-22; address applicant's claim 15) or processed food (see column 26, lines 43-44).

To one skilled in the art at the time of the invention would have found it obvious to combine the method of Moore et al. and wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or phenethyl isothiocyanate (PEITC) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement because Ghai et al. teaches a method of treating diseases by administering phenethyl isothiocyanate in a dietary composition or supplement (see abstract in its entirety; column 24, table I, line 6; column 25, lines 21-22; and column 26, lines 43-44).

The motivation to combine the method of Moore et al. and wherein the ITC-based agent is N-acetylcysteine conjugate of phenethyl isothiocyanate (PEITC-NAC) or phenethyl isothiocyanate (PEITC) or wherein the ITC-based agent is administered systemically in a dietary composition or supplement is because Ghai et al. teaches that PEITC treats diseases by activating the immune system (see column 3, lines 54-55 and

59-61). Additionally, Ghai et al. teaches that PEITC is isolated from a food substance and can be administered in processed foods or supplements.

(3) Claim 5, 9, and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sherr et al. (US 6,407,062 B1)) as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above and in view of Horan et al. (US 5,665,328).

Sherr et al. teaches are as applied to claims 1, 3, 4, 6, 8, 13, 14, 16, 19, and 23-26 above.

Sherr et al. does not teach a method wherein the ITC-based agent activates or augments a NK cell system.

Horan et al. teaches methods enabling binding bio-particle compounds to eukaryotic, prokaryotic cells and viruses, and to the use of the resultant particles for producing a site-specific predetermined therapeutic effect, in vivo (see column 1, lines 10-22). The bio-affecting substance has the formula R-B-R_1, wherein an addition reaction between "B" and an isothiocyanate functionality (see column 12, lines 36-39). The invention allows the lymphocyte NK-cells to recognize, bind to and kill a target tumor cell (see column 28, lines 55-56).

To one of ordinary skill in the art at the time of the invention would have found it obvious to combine the method of Sherr et al. and a method wherein the ITC-based agent activates or augments a NK cell system because Horan et al. teaches isothiocyanate compounds that allow the lymphocyte NK-cells to recognize, bind to and kill a target tumor cell (see column 28, lines 55-56).

The motivation to combine the method of Sherr et al. and a method wherein the ITC-based agent activates or augments a NK cell system is because both Horan et al. (see column 28, lines 55-56) and Sherr et al. (see column 22, lines 15-17 and see column 8, lines 59-65) teach isothiocyanate compounds that activate lymphocyte cells to treat tumors.

Conclusion

No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kendra D. Carter whose telephone number is (571) 272-9034. The examiner can normally be reached on 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KDC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER